REMARKS

Claims 84 to 94 are pending and under examination in the present application.

Claim 84 has been amended to recite SEQ ID NO:s from the Sequence Listing. Applicants thus assert that no new matter is being added with this amendment and request entry of the amendment.

I. Priority Claim

The Examiner has objected to the priority statement as lacking the patent number for all earlier filed applications. Applicants have amended the priority statement to reflect the patent number of U.S. App. No. 09/717,888, and thus respectfully request withdrawal of the objection.

II. Objection to Specification

The Examiner has objected to the specification because the abstract contains more than one paragraph. Applicants have amended the abstract so that it is in the form of a single paragraph and thus respectfully request withdrawal of the objection.

III. Rejection under the Judicially Created Doctrine of Non-statutory Obviousness Type Double Patenting

The Examiner has rejected claim 84 on the grounds of obviousness type double patenting as being unpatentable over claim 9 of U.S. Pat. No. 6,417,429. Specifically, the Examiner alleges that the subject matter of the claims is so closely related that they incorporate overlap species and/or claim 9 of the '429 patent is so broadly drafted that it incorporates any and all of the species that are present in the current application. Arguing along similar lines, the Examiner has also rejected claim 84 on the grounds of obviousness type double patenting as being unpatentable over claims 1 and 27 of U.S. Pat. No. 6,852,319. Applicants respectfully traverse the rejection and its supporting remarks.

The Examiner appears to believe that the mere fact that some species fall within the scope of both sets of claims and that the patented claims describe a genus which includes all species claimed by the pending claims is enough to support a rejection for non-statutory obviousness type double patenting. However, this is simply not the law. This type of rejection is only valid if the pending claims of an application are obvious variants or not patentably distinct from the claims of an issued patent. MPEP § 804(II)(B)(1).

Applicants respectfully assert that the pending claims are not obvious variants of the patented claims. For the Examiner's convenience, tables comparing pending claim 1 and the patented claims are provided below:

Pending Claim 1	U.S. Pat. No. 6,417,429 Claim 9
A method of producing a transgenic plant expressing an ***immunoglobulin comprising*** a ***protection protein in association with an immunoglobulin heavy chain*** having at least a portion of an antigen binding domain, wherein the protection protein comprises a portion of SEQ ID NO: 2, 4, 6, 8, or 10, comprising:	9. A method for making a transgenic plant capable of producing ***immunoglobulin molecules***, comprising:
a) introducing into a first plant an expression vector containing a nucleotide sequence encoding the ***protection protein*** operably linked to a transcriptional promoter,	(a) introducing into the genome of a first member of a plant species a first mammalian nucleotide sequence encoding an ***immunoglobulin heavy chain portion-containing polypeptide*** including a leader sequence forming a secretion signal, to produce a first transformant;
b) introducing into a second plant an expression vector containing a nucleotide sequence encoding the ***immunoglobulin heavy chain*** having at least a portion of an antigen binding domain operably linked to a transcriptional promoter,	(b) introducing into the genome of a second member of said plant species a second mammalian nucleotide sequence encoding an ***immunoglobulin light chain portion-containing polypeptide*** including a leader sequence forming a secretion signal, to produce a second transformant;

c) crossing said first plant and said second plant to produce offspring, and	(c) cross-pollinating said first and second transformants to generate a progeny population; and
d) selecting from said offspring a transgenic plant expressing the immunoglobulin comprising the protection protein in association with the immunoglobulin heavy chain having at least a portion of an antigen binding domain.	(d) isolating from said progeny population a transgenic plant species producing an immunoglobulin molecule, wherein said leader sequence is cleaved from said immunoglobulin molecules following proteolytic processing.

Pending Claim 1	U.S. Pat. No. 6,852,319 Claim 1
A method of producing a transgenic plant expressing an ***immunoglobulin comprising a protection protein in association with an immunoglobulin heavy chain*** having at least a portion of an antigen binding domain, wherein the protection protein comprises a portion of SEQ ID NO: 2, 4, 6, 8, or 10, comprising:	1. A method of passively immunizing a human or non-human animal subject against a preselected antigen using an ***immunoglobulin molecule*** produced in transgenic plants, said method comprising
a) introducing into a first plant an expression vector containing a nucleotide sequence encoding the ***protection protein*** operably linked to a transcriptional promoter, b) introducing into a second plant an expression vector containing a nucleotide sequence encoding the ***immunoglobulin heavy chain*** having at least a portion of an antigen binding domain operably linked to a transcriptional promoter, c) crossing said first plant and said second plant to produce offspring, and d) selecting from said offspring a transgenic plant expressing the immunoglobulin comprising the protection protein in association with	(a) obtaining a source of antigen-specific immunoglobulin from transgenic plant cells producing antigen specific immunoglobulin, said plant cells containing nucleotide sequences encoding an ***immunoglobulin heavy chain polypeptide and an immunoglobulin light chain polypeptide*** wherein said nucleotide sequences also encode a leader sequence for each polypeptide wherein each leader sequence forms a secretion signal that is cleaved from each of said immunoglobulin heavy chain and light chain polypeptides following proteolytic processing; and

the immunoglobulin heavy chain having at least a portion of an antigen binding domain.	
	(b) administering therapeutic amount of said antigen-specific immunoglobulin molecule to said subject, thereby passively immunizing a human or non-human animal subject against a preselected antigen.

Pending Claim 1	U.S. Pat. No. 6,852,319 Claim 27
A method of producing a transgenic plant expressing an ***immunoglobulin comprising*** a ***protection protein in association with an immunoglobulin heavy chain*** having at least a portion of an antigen binding domain, wherein the protection protein comprises a portion of SEQ ID NO: 2, 4, 6, 8, or 10, comprising:	27. A method of passively immunizing a human or non-human animal subject against a preselected antigen by administering an ***immunoglobulin*** produced by transgenic plant cells, said method comprising
a) introducing into a first plant an expression vector containing a nucleotide sequence encoding the ***protection protein*** operably linked to a transcriptional promoter, b) introducing into a second plant an expression vector containing a nucleotide sequence encoding the ***immunoglobulin heavy chain*** having at least a portion of an antigen binding domain operably linked to a transcriptional promoter, c) crossing said first plant and said second plant to produce offspring, and d) selecting from said offspring a transgenic plant expressing the immunoglobulin comprising the protection protein in association with the immunoglobulin heavy chain having	obtaining a formulation comprising an antigen-specific immunoglobulin by processing plant cells containing nucleotide sequences encoding an ***immunoglobulin heavy chain and an immunoglobulin light chain*** wherein said nucleotide sequences also encode a leader sequence for said heavy chain and said light chain and wherein each leader sequence forms a secretion signal that is cleaved from each of said immunoglobulin heavy chain and light chain polypeptides following proteolytic processing and

at least a portion of an antigen binding domain.	
	administering to said subject a therapeutic amount of said formulation comprising said antigen-specific immunoglobulin produced from transgenic plants.

As shown above, pending claim 84 is directed to methods of producing a transgenic plant expressing an immunoglobulin comprising a protection protein in association with an immunoglobulin heavy chain having at least a portion of an antigen binding domain, where the protection protein comprises a portion of SEQ ID NO: 2, 4, 6, 8, or 10 by introducing into a plant an expression vector containing a nucleotide sequence encoding the protection protein, introducing into a second plant an expression vector containing a nucleotide sequence encoding the immunoglobulin heavy chain having at least a portion of an antigen binding domain, crossing the two plants, and selecting transgenic plants.

Claim 9 of the '419 patent is directed to methods of making transgenic plants capable of producing immunoglobulin molecules by introducing into a plant a nucleotide sequence encoding a immunoglobulin heavy chain portion-containing polypeptide including a leader sequence forming a secretion signal, introducing into a second plant a nucleotide sequence encoding a immunoglobulin heavy chain portion-containing polypeptide including a leader sequence forming a secretion signal, cross-pollinating the two plants, and isolating transgenic plants. Claims 1 and 27 of the '319 patent are directed to methods of passive immunization using immunoglobulin molecules produced in transgenic plants, where the methods involve obtaining the molecules from plant cells containing nucleotide sequences encoding the immunoglobulin heavy chain, a light chain, and leader sequences forming a secretion signal.

Thus, the pending claims are directed to methods of making transgenic plants expressing a protection protein in association with an immunoglobulin heavy chain, while the patented claims are directed to methods for production of immunoglobulin molecules comprising an

immunoglobulin heavy chain and light chain portion-containing polypeptides using plants and methods for use of such immunoglobulin molecules.

The invention disclosed and claimed in the present invention is a method of producing a complex of at least two proteins: (1) an immunoglobulin heavy chain and (2) protection protein, which comprises at least a portion of a polyimmunoglobulin receptor. Each of these proteins is a mammalian protein which is normally expressed in cells of the mammalian immune system. Furthermore, each of these proteins is a highly structured protein with a very specific folded three dimensional structure which is held together by disulfide bonds. Given the enormous differences in the machinery for the biosynthesis, correct folding, assembly of protein complexes, and glycosylation patterns in plant and animal cells, one would not know before making the invention whether this complex of proteins could be properly synthesized and assembled in a functional form in a plant cells, even in light of the patented claims to methods for expressing mammalian immunoglobulin molecules in plant cells.

Immunoglobulin heavy chains and protection proteins are molecules containing numerous cysteine residues that are disulfide bonded in specific pairings to form immunoglobulin domains. Disulfide bonding of incorrect pairs of cysteine residues can have profound effects on the structure, and thus function of the resulting protein and lead to a non-functional protein. It cannot be known or obvious *a priori* that the correct formation of multiple disulfide bonds would occur in plant cells. A variety of intracellular proteins such as heat shock proteins, chaperones, proline isomerases, as well other factors are required for correct protein folding. Whether plant cells had equivalent proteins that could correctly fold both of the proteins that form the immunoglobulin heavy chain/ protection protein complex would not have been known at the priority date of this invention without actually performing the experiment because of fundamental differences between plant cells and animal cells.

Even if these two proteins were correctly synthesized, properly folded and disulfide bonded, it would not be certain that the two proteins would be correctly assembled into a complex in plant cells. This is because not only is the biochemistry and physiology of plant and animal cells

different, but the cellular compartments in which protein folding and assembly occur are different between plant and animal cells. These differences would allow ample opportunity for misfolding and assembly of non-native mammalian proteins to occur in plant cells.

Furthermore, at the priority date of this application, one of skill would have expected assembly of immunoglobulin heavy chain with protection protein to be a more complex process than that required for assembly of immunoglobulin heavy chain and light chain portion-containing polypeptides as described in the patented claims. Protection proteins of this invention are analogous to secretory component, both of which are derived from the N-terminal portion of the polymeric immunoglobulin receptor. In mammalian cells, assembly of secretory component with immunoglobulin chains occurs during transcytosis of the immunoglobulin into the specialized microenvironment provided by the mucosal cells. Given the close similarity between protection protein and secretory component, one of skill would have expected successful assembly of the immunoglobulin heavy chain with a protection protein to require a microenvironment as specialized as that required for assembly of immunoglobulin with secretory component. As discussed above, the differences in asssembly machinery in plant and animal cells are significant. In light of these differences and the known requirement for a specialized environment beyond that required for assembly of immunoglobulin molecules, it would have been surprising to one of skill that such complexes could be assembled in plant cells. It is Applicants who made the unexpected discovery that such complexes could indeed be assembled in plants, as demonstrated in Example 7 on page 92 of the specification.

In addition, at the priority date of this application, it was known that plants glycosylate proteins in a different pattern than do animal cells. Thus, one of skill in the art would expect that protein components of the present invention would be glycosylated in a pattern typical of plants, not animal cells. Such a glycosylation pattern would not be the native pattern as would be generated in animal cells. Because a correct, mammalian pattern of glycosylation was thought to be important, one of skill upon reading the patented claims could not have predicted that methods of this invention could be used to produce functional protein complexes of this invention.

Thus, in light of the known difficulties in producing functional mammalian protein complexes in plant cells and in particular, the specialized microenvironment expected to be required for assembly of protection protein with immunoglobulin heavy chain, the pending claims are not obvious in view of the claims in the above-cited patents. Applicants thus respectfully request that the Examiner withdraw the rejection for non-statutory obviousness type double patenting.

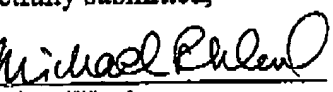
CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. **415142000303**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: May 26, 2006

Respectfully submitted,

By 

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